REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated November 28, 2008.

Status of the Claims

Claims 1, 3, 6, 21 and 22 pending in the present application. No claims have been amended or added by this response.

Claim Rejections – 35 USC § 112, First Paragraph

The Examiner rejects claims 1, 3, 6 and newly added claims 21-22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner again asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleges that one skilled in the art would not be able to determine which markers are essentially unique to the antibody-producing cells and that the instant specification does not clearly define which markers are 'predominantly present' and does not provide a standard to ascertain the degree of 'predominant presence'. The Examiner states that given the plethora of cell surface markers and the non-limiting definition of these 'essentially unique' markers, one skilled in the art cannot visualize or recognize the identity of the members of the genus of markers that exhibit this functional property.

Applicants respectfully traverse this rejection and assert that claims 1, 3, 6, 21 and 22 comply with the written description requirement. Applicants draw the Examiner's attention to the fact that the present method is a method of **ENRICHING** and not purification or isolation. The Examiner is reminded that to enrich is to: "to improve or increase the quality or value". In the context of the present invention, it is clear that enrich means to increase the number of cells which produce an antibody that recognizes an antigen of interest. The increase can be performed even if some other cells remain in the mix. Thus the definition of "essentially unique"

(ie which includes a marker that is predominantly present on those cells capable of producing antibody) is not incompatible with the purpose of the process of the invention. Furthermore, we consider that the Examiner's position that a skilled person would not able to determine which markers are essentially unique to the antibody producing cells is not in line with the practical reality of the ability of the skilled person, in light of the teaching of the present specification. In fact, all that is required is for the skilled person to consider which cell types are for consideration and then to do a literature search to identify a marker that is specific or very highly expressed on the relevant cells. Applicants assert that the specification conveys to the skilled artisan that Applicants were in possession of the invention as instantly claimed at the time of filing.

In view of the foregoing remarks, Applicants request that the Examiner's rejections under 35 U.S.C. 112, first paragraph, be withdrawn.

Claim Rejections – 35 USC § 103

Claims 1, 3, 6, and new claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US Patent 5,213,960) in view of Goldsby et al (*Kuby Immunology*, 4th edition, 2000, W.H. Freeman and Co., New York, USA. Pages 104 and 165-169) and Brezinsky et al (JIM 2003, 277:144-155, cited on IDS). Chang is cited as teaching an enrichment method using FACS comprising labeling a B cell marker with an antibody conjugated to a fluorescent label and the antigen of interest that is labeled with a second antibody conjugated to a fluorescent label. The Examiner notes that Chang differs from the present claims in that Chang's antigen was directly labeled with a fluorochrome whereas the antigen recited in the present claims is indirectly labeled by a polyclonal antibody that recognizes the antigen, wherein the polyclonal antibody was labeled with a fluorochrome. The Examiner alleges, however, that it would have been obvious to one of ordinary skill in the art at the time the invention was made to indirectly label the antigen with a polyclonal antibody because of the advantages offered by indirect labeling, and polyclonal antibody was evidenced by Goldsby et al. The Examiner further remarks that Chang differs from the present claims in that it does not explicitly teach "at least one wash step" in the enrichment method. The Examiner asserts, however, that it would have

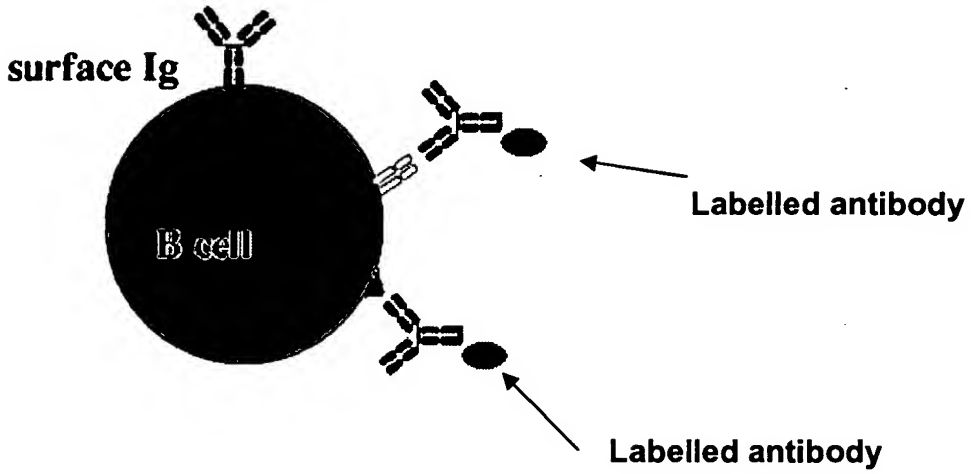
been obvious to a person of ordinary skill in the art to include at least one wash step in the method of enriching a population of cells using FACS because it was well known at the time of the invention to include wash steps in any immunoassays. Brezinsky et al is cited and applied as teaching washing antibody-producing cells before and after labeling in a method of enrichment FACS.

Applicants respectfully traverse this rejection. Applicants assert that claims 1, 3, 6, 21 and 22 are not made obvious by the combination of any combination of Chang, Goldsby et al, and Brezinsky et al. To establish obviousness, a prior art reference, or the combination of references, must teach or suggest each and every element and limitation of the claim(s). Chang, Goldsby et al and Brezinsky et al do not suggest each and every element of claims 1, 3, 6, 21 and 22. Chang *et al* (US 5,213,960) discloses:

> "*The sorting of B cells expressing antibodies.. by labeling* [said] *B cells with at least two antigen probes* [eg with two, three or four labeled antibodies]".
>
> Col 5 lines 23 to 26

This can be illustrated as shown below where a B cell which has many antigens/proteins **expressed on its surface** is labeled with at least two types of antibodies each with a distinct label. Please see Fig 1.

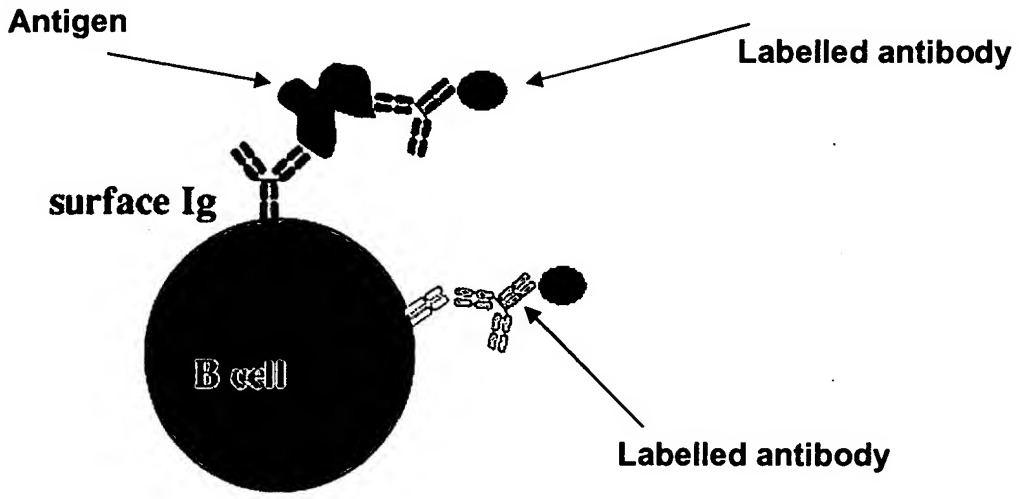
Figure 1:



One of the probes (ie labeled antibodies) can be directed to the part of the chain (Fc) of the surface immunoglobulin (Ig). It can be seen that all the labels in the method according to Chang are on the B cell.

In contrast, the present invention relates to a method of first targeting a marker (such as a protein) on a B cell with a labeled antibody specific for the marker, then bringing an antigen "specific" to a surface immunoglobulin (Ig) into contact with the cells. This antigen is unlabelled as is the surface Ig. This is important because it ensures that there is no interference with the natural binding of the surface Ig and the corresponding epitope on the antigen. Please see Fig 2.

Figure 2:



The next step is then to expose the cells to polyclonal antibodies specific to the antigen bound to the surface Ig. These polyclonal antibodies are labeled. It is respectfully submitted that the Examiner's statement that:

> *"The difference between Chang and the present claims was that the Chang's antigen was directly labeled with a fluorochrome whereas the antigen in the present claims was indirectly labeled with a polycolonal antibody that recognized the antigen"*

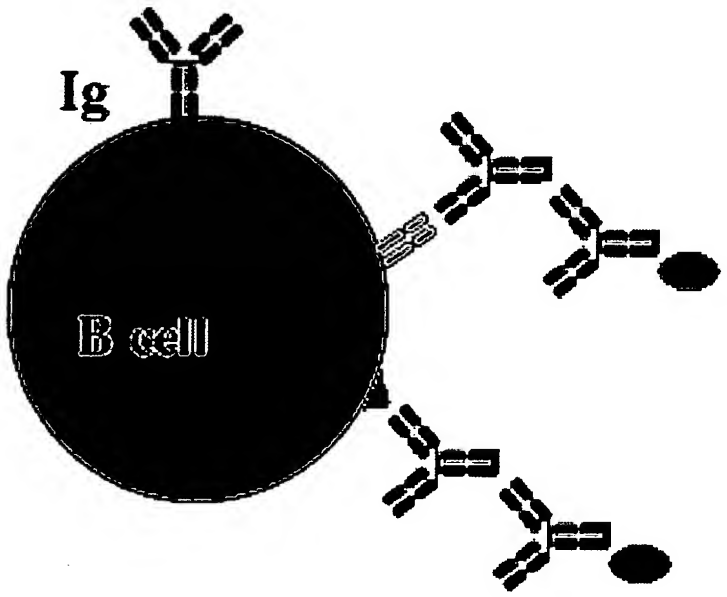
is not necessarily an accurate assessment of the difference between the prior art and the present claimed invention. We suggest that Chang teaches a skilled person to use two or more labeled antibodies to label antigens on the surface of a B cell. One of the antibodies may be directed at part of the constant region (Fc) of the surface immunoglobulin. This would only identify antibodies of a certain sub-type and does not necessarily identify only those or all those antibodies against a particular target antigen or epitope.

In contrast, the present method identifies those cells where the surface Ig has bound to the target antigen. There are at least three advantages associated with the present method. Namely, one advantage is that because the target antigen is unlabeled, then the natural binding/association of the antigen and the surface Ig is not disturbed, thereby optimizing the number of surface Ig

which will bind antigen and also be identified by subsequent labeling. In addition, as only cells where the surface Ig has bound the target antigen are labeled, the specificity of the present method is likely to be greatly improved in relation to the method of Chang. Furthermore, the use of the polyclonal antibodies ensures that the labeling generates a suitably amplified signal. It is respectfully submitted that there is no teaching or suggestion in Chang to provide an improved method according to the presently claimed invention. Therefore, the presently claimed invention is not obvious after consideration of Chang.

Goldsby *et al* describes general methods of indirect labeling, and it does **not** provide a teaching or suggestion to provide the method according to the presently claimed invention. In fact the combined teaching of Chang and Goldsby would provide the following arrangement (see Goldsby figure b) page 166):

Figure 3



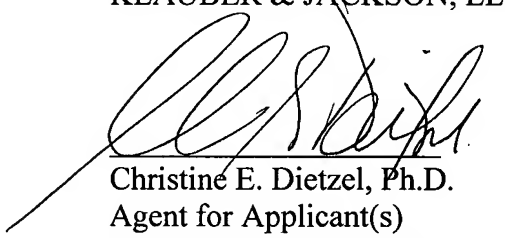
This does not provide the presently claimed invention. Furthermore, a combination with Brezinsky (which teaches multiple washing steps) also does not provide the presently claimed invention. Applicants respectfully submit that claims 1, 3, 6, 21 and 22 are not made obvious by the combination of any combination of Chang, Goldsby et al, and Brezinsky et al.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C.103 (a) may properly be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,
KLAUBER & JACKSON, LLC



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